WEST Search History

DATE: Wednesday, September 25, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB; PLUR=YES; OP=ADJ			
L3	L2 and vaccinia	13	L3
L2	GAD and diabetes	169	L2
L1	GAD and diadetes	0	L1

END OF SEARCH HISTORY

10/7/1
DIALOG(R)File 155:MEDLINE(R)

14412438 22417945 PMID: 12530520
Role of glutamic acid decarboxylase in the pathogenesis of type 1 diabetes.
Jun H S; Khil L Y; Yoon J W
Laboratory of Viral and Immunopathogenesis of Diabetes, Julia McFarlane Diabetes Research Centre, Department of Microbiology and Infectious Diseases, Faculty of Medicine, The University of Calgary, Calgary, Alberta T2N 4N1, Canada.
Cellular and molecular life sciences - CMLS (Switzerland) Nov 2002, 59 (11) p1892-901, ISSN 1420-682X Journal Code: 9705402
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Glutamic acid decarboxylase (GAD) is considered to be one of the strongest candidate autoantigens involved in triggering beta-cell-specific autoimmunity. The majority of recent onset type 1 diabetes patients and pre-diabetic subjects have anti-GAD antibodies in their sera, as do nonobese diabetic (NOD) mice, one of the best animal models for human type I diabetes. Immunization of young NOD mice with GAD results in the prevention or delay of the disease as a result of tolerizing autoreactive T cells. Autoimmune diabetes can also be prevented by the suppression of GAD expression in antisense GAD transgenic mice backcrossed with NOD mice for seven generations. These results support the hypothesis that GAD plays an important role in the development of T-cell-mediated autoimmune diabetes. However, there is some controversy regarding the role of GAD in the pathogenesis of diabetes. Whether GAD truly plays a key role in the initiation of this disease remains to be determined. The examination of the development of insulitis and diabetes in beta-cell-specific GAD knockout NOD mice will answer this remaining question. (128 Refs.)
Record Date Created: 20030117
Record Date Completed: 20030205

10/7/2
DIALOG(R)File 155:MEDLINE(R)

11723375 99160052 PMID: 10052687
Type 1 1/2 diabetes: myth or reality?
Juneja R; Palmer J P
Department of Veteran Affairs Puget Sound Health Care System, University of Washington, Endocrinology, Seattle 98108, USA. rjun@u.washington.edu
Autoimmunity (SWITZERLAND) 1999, 29 (1) p65-83, ISSN 0891-6934 Journal Code: 8900070
Contract/Grant No.: M01-RR-00037; RR; NCRR; P30-DK17047; DK; NIDDK
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The disease process in classical Type 1 diabetes patients (IDDM) is believed to be autoimmune. In contrast, the disease process in classical Type 2 diabetes patients (NIDDM) is not autoimmune and a decreased sensitivity to insulin action is the main abnormality. The clinical distinction of Type 1 diabetes versus Type 2 diabetes is recognized to be imperfect and has limitations. There is a group of individuals (Type 1 1/2 diabetes), who present like typical NIDDM, but have some of the

immunological and clinical features of IDDM. We review the current medical literature on Type 1 1/2 diabetes with special reference to its clinical characteristics, natural history and pathophysiology. Since the distinction between these two forms of diabetes may have important therapeutic implications especially with regards to the benefits of insulin therapy in patients with Type 1 1/2 diabetes and because of the need for uniformity in its diagnosis we recommend that both clinical plus biochemical criteria (the presence of ICA and/or GAD Ab, HLA typing and tests to quantify beta cell function) be used to make a diagnosis. Comparative studies in the area of cytokine production, T cell reactivity and autoantibody clustering between classic Type 1 diabetes and Type 1 1/2 diabetes patients are needed as are studies with the animal model of Type 1 1/2 diabetes, Psammomys obesus. (143 Refs.)
Record Date Created: 19990510
Record Date Completed: 19990510

10/7/3
DIALOG(R)File 155:MEDLINE(R)

11600601 99033259 PMID: 9816471
Vesicular autoantigens of type 1 diabetes.
Solimena M
Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520-8020, USA.
Diabetes/metabolism reviews (UNITED STATES) Sep 1998, 14 (3) p227-40, ISSN 0742-4221 Journal Code: 8601109
Contract/Grant No.: DK-53022; DK; NIDDK
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Type 1 diabetes, also referred to as insulin-dependent diabetes mellitus (IDDM), is an autoimmune disorder resulting from the destruction of pancreatic beta-cells and insulin deficiency. In the last 10 years significant progress has been made in this field, primarily because of the identification of predisposing genes, the extensive investigation of animal models, and the characterization of major autoantigens. This review draws attention to how the study of beta-cell autoantigens may contribute insight into the pathogenesis of IDDM and provides an update on the cell biology of glutamic acid decarboxylase (GAD) and islet cell autoantigen 512, two major targets of autoimmunity in Type 1 diabetes on which I have focused my efforts. For reasons of space I have mostly considered here studies on GAD which have been published since 1994. (91 Refs.)
Record Date Created: 19990107
Record Date Completed: 19990107

10/7/4
DIALOG(R)File 155:MEDLINE(R)

10503131 96313712 PMID: 8768297
[Autoimmunity and glutamate decarboxylase antibodies in the pathogenesis of type I diabetes mellitus in experimental and clinical practice]
Autoimunita a protilatky proti glutamatdekarboxylaze v patogenezi diabetes mellitus I. typu v experimentu a klinicke praxi.
Kucera P; Andel M; Treslova L
Oddeleni alergologie a klinicke imunologie FN Kralovske Vinohrady, Praha.
Vnitrni lekarstvi (CZECH REPUBLIC) May 1996, 42 (5) p359-67, ISSN 0042-773X Journal Code: 0413602

Document type: Journal Article; Review; Review Literature ; English Abstract
Languages: CZECH
Main Citation Owner: NLM
Record type: Completed

Diabetes mellitus type 1 (DM type 1) is a chronic, organ specific autoimmune disease. Autoantibodies against the islets of Langerhans (ICA) are found in 71%, against insulin (IA) in 65% against glutamate decarboxylase (GAD) in 67-77% of children with DM type 1; in their close relatives and in patients with a more prolonged persistence of DM type 1 these antibodies and manifestations of cell-mediated autoreactivity are found less frequently also as a sign of the autoimmune character of DM type 1. In the pathogenesis of DM type 1 with the help of experimental mammalian models an idea on the genesis of the disease was obtained--activation of autoimmunity on the background of genetic sensitivity and environmental factors, the development of lymphocytic infiltration of the pancreatic islets (insulitis) destruction of pancreatic B-cells due to the cytotoxicity of T lymphocytes and the manifestation of DM type 1. According to this idea among the series of antigens of B-cells of the islets of Langerhans the dominant antigen is the isoform GAD65--under experimental conditions the specific response of T lymphocytes against GAD65 is found first, then follows extension of the reactivity also against other antigens of the islets. Understanding of the immune pathogenesis of DM type 1 makes it possible to apply the immunomodulating approach to the treatment of this condition which gave the first positive results in experimental work as well as in clinical practice. (65 Refs.)

Record Date Created: 19960924
Record Date Completed: 19960924

10/7/5
DIALOG(R)File 155:MEDLINE(R)

09842517 21653818 PMID: 11795511

Cellular and molecular pathogenic mechanisms of insulin-dependent diabetes mellitus.

Yoon J W; Jun H S

Department of Microbiology and Infectious Disease, Julia McFarlane Diabetes Research Centre, Faculty of Medicine, The University of Calgary, Alberta, Canada. yoon@ucalgary.ca

Annals of the New York Academy of Sciences (United States) Apr 2001, 928 p200-11, ISSN 0077-8923 Journal Code: 7506858

Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Insulin-dependent diabetes mellitus (IDDM), also known as type 1 diabetes, is an organ-specific autoimmune disease resulting from the destruction of insulin-producing pancreatic beta cells. The hypothesis that IDDM is an autoimmune disease has been considerably strengthened by the study of animal models such as the BioBreeding (BB) rat and the nonobese diabetic (NOD) mouse, both of which spontaneously develop a diabetic syndrome similar to human IDDM. Beta cell autoantigens, macrophages, dendritic cells, B lymphocytes, and T cells have been shown to be involved in the pathogenesis of autoimmune diabetes. Among the beta cell autoantigens identified, glutamic acid decarboxylase (GAD) has been extensively studied and is the best characterized. Beta cell-specific suppression of GAD expression in NOD mice results in the prevention of IDDM. Macrophages and/or dendritic cells are the first cell types to infiltrate the pancreatic islets. Macrophages play an essential role in the development and activation of beta cell-cytotoxic T cells. B lymphocytes

play a role as antigen-presenting cells, and T cells have been shown to play a critical role as final effectors that kill beta cells. Cytokines secreted by immunocytes, including macrophages and T cells, may regulate the direction of the immune response toward Th1 or Th2 as well as cytotoxic effector cell or suppressor cell dominance. Beta cells are destroyed by apoptosis through Fas-Fas ligand and TNF-TNF receptor interactions and by granzymes and perforin released from cytotoxic effector T cells. Therefore, the activated macrophages and T cells, and cytokines secreted from these immunocytes, act synergistically to destroy beta cells, resulting in the development of autoimmune IDDM. (52 Refs.)

Record Date Created: 20020117

Record Date Completed: 20020222

10/7/6

DIALOG(R)File 155:MEDLINE(R)

09735136 21536612 PMID: 11679421

International Workshop on Lessons From Animal Models for Human Type 1 Diabetes: identification of insulin but not glutamic acid decarboxylase or IA-2 as specific autoantigens of humoral autoimmunity in nonobese diabetic mice.

Bonifacio E; Atkinson M; Eisenbarth G; Serreze D; Kay T W; Lee-Chan E; Singh B

Department of Medicine, Isituto Scientifico San Raffaele, Milan, Italy.

Diabetes (United States) Nov 2001, 50 (11) p2451-8, ISSN 0012-1797 Journal Code: 0372763

Document type: Consensus Development Conference; Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Several self-antigens have been reported as targets of the autoimmune response in nonobese diabetic (NOD) mice. The aim of this workshop was to identify autoantibody assays that could provide useful markers of autoimmunity in this animal model for type 1 diabetes. More than 400 serum samples from NOD (4, 8, and 12 weeks of age and at diabetes onset), BALB/c, and B6 mice were collected from six separate animal facilities, coded, and distributed to five laboratories for autoantibody measurement. Insulin autoantibodies (IAA) were measured by radiobinding assay (RBA) by four laboratories and by enzyme-linked immunosorbent assay (ELISA) in one laboratory. Using the 99th percentile of BALB/c and B6 control mice as the threshold definition of positivity, IAA by RBA were detected in NOD mice at frequencies ranging from 10 to 30% at age 4 weeks, from 26 to 56% at 8 weeks, from 42 to 56% at 12 weeks, and from 15 to 75% at diabetes onset. With ELISA, IAA signals differed significantly between control mouse strains and increased with age in both control and NOD mice, with frequencies in NOD animals being 0% at 4 weeks, 14% at 8 weeks, 19% at 12 weeks, and 42% at diabetes onset. For IAA, the ELISA results were relatively discordant with those of RBA. GAD autoantibody (GADA) and IA-2 autoantibody (IA-2A) signals obtained by RBA were low (maximum 2.5% of total) but were increased in NOD mice compared with control mice at diabetes onset (GADA 29-50%; IA-2A 36-47%). ELISA also detected GADA (42%) and IA-2A (50%) at diabetes onset, with results concordant with those of RBA. Remarkably, GADA and IA-2A frequencies varied significantly with respect to the source colony of NOD mice. Furthermore, whereas neither GADA nor IA-2A correlated with IAA, there was strong concordance between GADA and IA-2A in individual mice. Sera with increased binding to GAD and IA-2 also had increased binding to the unrelated antigen myelin oligodendrocyte glycoprotein, and binding to GAD could not be inhibited with excess unlabeled antigen, suggesting nonspecific interactions. In sum, this workshop demonstrated that IAA measured by sensitive RBA are a marker of

autoimmunity in NOD mice and draw into question the true nature of GADA and IA-2A in this animal model. (22 Refs.)
Record Date Created: 20011026
Record Date Completed: 20011207

10/7/7
DIALOG(R)File 155:MEDLINE(R)

09449306 21221399 PMID: 11324686
Genetic and immunological basis of autoimmune diabetes in the NOD mouse.
Yoshida K; Kikutani H
Department of Molecular Immunology, Research Institute for Microbial Diseases, Osaka University, Japan.
Reviews in immunogenetics (Sweden) 2000, 2 (1) p140-6, ISSN 1398-1714 Journal Code: 100883703
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The non-obese diabetic (NOD) mouse is an animal model of human insulin-dependent diabetes mellitus (IDDM). Most NOD mice show insulitis at several weeks of age, and 60-90% of the female mice develop overt diabetes after 20-30 weeks of age. NOD mice share many features of human IDDM. As in human IDDM, the disease development in NOD mice is controlled by a number of disease susceptibility or resistant genes (Idds), including the major histocompatibility complex locus. Cumulative evidence suggests that Thl CD4+ T cells play a critical role in the autoimmune process leading to beta cell destruction. In addition to CD4+ T cells, CD8+ cells and B cells also participate in the pathogenesis. There are several candidate antigens recognized by autoreactive T cells such as glutamic acid decarboxylase (GAD), insulin and heat shock protein (HSP) 60. Treatment by these antigens suppresses IDDM development in NOD mice, suggesting that they may initiate the autoimmune process of NOD mice. (70 Refs.)
Record Date Created: 20010427
Record Date Completed: 20010531

10/7/8
DIALOG(R)File 155:MEDLINE(R)

08763408 20044588 PMID: 10576760
Autoimmune diabetes: is GAD the culprit?
Lopez-Liuchi J V
Division d'Endocrinologie et Diabetologie, Departement de Medecine Interne, Hopital Universitaire de Geneve, Rue Micheli-du-Crest 24, 1211 Geneva 14, Switzerland.
European journal of endocrinology / European Federation of Endocrine Societies (ENGLAND) Nov 1999, 141 (5) p458-9, ISSN 0804-4643 Journal Code: 9423848
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
(8 Refs.)
Record Date Created: 19991228
Record Date Completed: 19991228

10/7/9

08735922 20015762 PMID: 10549569

Cellular and molecular roles of beta cell autoantigens, macrophages and T cells in the pathogenesis of autoimmune diabetes.

Yoon J W; Jun H S

Dept. of Microbiology and Infectious Disease, Faculty of Medicine, The University of Calgary, Alberta, Canada. yoon@ucalgary.ca

Archives of pharmacal research (KOREA (SOUTH)) Oct 1999, 22 (5) p437-47, ISSN 0253-6269 Journal Code: 8000036

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Type I diabetes, also known as insulin-dependent diabetes mellitus (IDDM) results from the destruction of insulin-producing pancreatic beta cells by a progressive beta cell-specific autoimmune process. The pathogenesis of autoimmune IDDM has been extensively studied for the past two decades using animal models such as the non-obese diabetic (NOD) mouse and the BioBreeding (BB) rat. However, the initial events that trigger the immune responses leading to the selective destruction of the beta cells are poorly understood. It is thought that beta cell autoantigens are involved in the triggering of beta cell-specific autoimmunity. Among a dozen putative beta cell autoantigens, glutamic acid decarboxylase (GAD) has been proposed as perhaps the strongest candidate in both humans and the NOD mouse. In the NOD mouse, GAD, as compared with other beta cell autoantigens, provokes the earliest T cell proliferative response. The suppression of GAD expression in the beta cells results in the prevention of autoimmune diabetes in NOD mice. In addition, the major populations of cells infiltrating the islets during the early stage of insulitis in BB rats and NOD mice are macrophages and dendritic cells. The inactivation of macrophages in NOD mice results in the prevention of T cell mediated autoimmune diabetes. Macrophages are primary contributors to the creation of the immune environment conducive to the development and activation of beta cell-specific Th1-type CD4+ T cells and CD8+ cytotoxic T cells that cause autoimmune diabetes in NOD mice. CD4+ and CD8+ T cells are both believed to be important for the destruction of beta cells. These cells, as final effectors, can kill the insulin-producing beta cells by the induction of apoptosis. In addition, CD8+ cytotoxic T cells release granzyme and cytolysin (perforin), which are also toxic to beta cells. In this way, macrophages, CD4+ T cells and CD8+ T cells act synergistically to kill the beta cells in conjunction with beta cell autoantigens and MHC class I and class II antigens, resulting in the onset of autoimmune type I diabetes. (113 Refs.)

Record Date Created: 20000124

Record Date Completed: 20000124

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9/7/1
DIALOG(R)File 155:MEDLINE(R)

09735136 21536612 PMID: 11679421

International Workshop on Lessons From Animal Models for Human Type 1 Diabetes: identification of insulin but not glutamic acid decarboxylase or IA-2 as specific autoantigens of humoral autoimmunity in nonobese diabetic mice.

Bonifacio E; Atkinson M; Eisenbarth G; Serreze D; Kay T W; Lee-Chan E; Singh B

Department of Medicine, Isituto Scientifico San Raffaele, Milan, Italy.

Diabetes (United States) Nov 2001, 50 (11) p2451-8, ISSN 0012-1797
Journal Code: 0372763
Document type: Consensus Development Conference; Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Several self-antigens have been reported as targets of the autoimmune response in nonobese diabetic (NOD) mice. The aim of this workshop was to identify autoantibody assays that could provide useful markers of autoimmunity in this animal model for type 1 diabetes. More than 400 serum samples from NOD (4, 8, and 12 weeks of age and at diabetes onset), BALB/c, and B6 mice were collected from six separate animal facilities, coded, and distributed to five laboratories for autoantibody measurement. Insulin autoantibodies (IAA) were measured by radiobinding assay (RBA) by four laboratories and by enzyme-linked immunosorbent assay (ELISA) in one laboratory. Using the 99th percentile of BALB/c and B6 control mice as the threshold definition of positivity, IAA by RBA were detected in NOD mice at frequencies ranging from 10 to 30% at age 4 weeks, from 26 to 56% at 8 weeks, from 42 to 56% at 12 weeks, and from 15 to 75% at diabetes onset. With ELISA, IAA signals differed significantly between control mouse strains and increased with age in both control and NOD mice, with frequencies in NOD animals being 0% at 4 weeks, 14% at 8 weeks, 19% at 12 weeks, and 42% at diabetes onset. For IAA, the ELISA results were relatively discordant with those of RBA. GAD autoantibody (GADA) and IA-2 autoantibody (IA-2A) signals obtained by RBA were low (maximum 2.5% of total) but were increased in NOD mice compared with control mice at diabetes onset (GADA 29-50%; IA-2A 36-47%). ELISA also detected GADA (42%) and IA-2A (50%) at diabetes onset, with results concordant with those of RBA. Remarkably, GADA and IA-2A frequencies varied significantly with respect to the source colony of NOD mice. Furthermore, whereas neither GADA nor IA-2A correlated with IAA, there was strong concordance between GADA and IA-2A in individual mice. Sera with increased binding to GAD and IA-2 also had increased binding to the unrelated antigen myelin oligodendrocyte glycoprotein, and binding to GAD could not be inhibited with excess unlabeled antigen, suggesting nonspecific interactions. In sum, this workshop demonstrated that IAA measured by sensitive RBA are a marker of autoimmunity in NOD mice and draw into question the true nature of GADA and IA-2A in this animal model. (22 Refs.)

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Set      Items    Description
S1       15244    DIABETES AND MODEL?
S2      944443    DT=REVIEW?
S3        2329    S1 AND S2
S4         955    S1/TI AND S2
S5           2    CAUTION AND S4
S6         152    ANIMAL(W)MODEL?/TI AND DIABETES/TI
S7          41    S2 AND S6
S8        2976    GAD
S9           1    S6 AND S8
S10          9    S4 AND S8
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Set	Items	Description
S1	15244	DIABETES AND MODEL?
S2	944443	DT=REVIEW?
S3	2329	S1 AND S2
S4	955	S1/TI AND S2
S5	2	CAUTION AND S4
S6	152	ANIMAL(W)MODEL?/TI AND DIABETES/TI
S7	41	S2 AND S6
S8	2976	GAD
S9	1	S6 AND S8

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